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RESPONSE UNDER 37 CFR 1.110

EXPEDITED PROCEDURE

EXAMINING GROUP 1643

inflammatory bowel disease, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 16.

Please cancel claim 18.

REMARKS

Reconsideration of the present application in view of the foregoing amendments and the following remarks is respectfully requested.

Claims 2 to 22 are pending in the present application. Claims 7, 9, 10, 13, 14, 16 and 17 have been amended herein. As the amendments remove issues for appeal, Applicant respectfully requests entry thereof. MPEP § 714.13. No new claims have been added, and claim 18 has been cancelled.

Applicants acknowledge with appreciation the withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, as well as certain rejections under 35 U.S.C. §§ 102 and 112, second paragraph. Applicants also acknowledge with appreciation the Examiner's ruling that claims 9, 13 and 14 would be allowable if rewritten to overcome the rejections under 35 U.S.C. § 112, second paragraph and to include all limitations of the base and intervening claims.

Alleged Indefiniteness

RESPONSE UNDER 37 C.F.R.
EXPEDITED PROSECUTION
EXAMINING GROUP

A. Claims 2 to 22 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for recitation of the term “solvates.” Applicants respectfully submit that, when read in light of the specification, the term “solvates” conveys a clear and definite meaning to the skilled artisan. Nevertheless, to advance prosecution and to further clarify the subject matter that Applicants regard as their invention, the term “solvates” has been deleted from claims 14 and 16. Support for the amendment is found throughout the specification. Applicants submit that the rejection has been obviated, and request withdrawal thereof.

B. Claims 2 to 13 and 15 to 22 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for recitation of various “optionally substituted” groups. Applicants respectfully submit that the boundaries of patent protection sought are clearly set forth in the cited claims, and the claims describe the claimed subject matter with a reasonable degree of precision and particularity, which is all the law requires. *In re Mercier*, 515 F.2d 1161, 1268 (C.C.P.A. 1975); *In re Barr*, 444 F.2d 588 (C.C.P.A. 1971). Nevertheless, to advance prosecution, and to further clarify the subject matter that Applicants regard as their invention, claims 7, 9, 10, 13 and 16 have been amended to enumerate particular substituents for the optionally substituted groups recited therein. Support for the amendments is found in the specification at, for example, page 6, lines 5 to 8; page 7, line 5 to page 8, line 4; page 10, line 27 to page 11, line 3; page 12, lines 3 to 33; page 13, line 14 to page 14, line 4; page 15, lines 22 to 24; and page 17, line 35 to page 18, line 2. Applicants submit that the rejection has been obviated, and request withdrawal thereof.

RESPONSE UNDER 37 CFR
EXPEDITED PROCESSING
EXAMINING CORRESPONDENCE

C. Claims 2 to 13 and 15 to 22 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for recitation of the terms “heteroaliphatic group,” “cycloaliphatic group,” “polycycloaliphatic group,” and “heteropolycycloaliphatic group.” More specifically, the Office Action asserts that the terms are “oxymorons” because the prefixes allegedly conflict with the stem word “aliphatic.” Applicants traverse because the cited terminology conveys a clear and definite meaning to one of ordinary skill in the art of organic chemistry, and the skilled artisan would thus understand the metes and bounds of the claims.

A fundamental principle of 35 U.S.C. § 112, second paragraph is that patent Applicants are entitled to be their own lexicographers and may define the claims in whatever terms they so choose. M.P.E.P. § 2173.01. Accordingly, “[t]he examiner’s focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. 112, second paragraph is whether the claim meets the threshold requirements of clarity and precision, *not whether more suitable language or modes of expression are available.*” M.P.E.P. § 2173.02 (emphasis added). The language employed by Applicants defines the patentable subject matter in a manner that one of ordinary skill in the art would understand, which is all that is required to satisfy 35 U.S.C. § 112, second paragraph. *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372 (Fed. Cir. 2000). Thus, even if the terms used by Applicants are “oxymorons” (which Applicants do not concede), this fact alone would not be sufficient to support the present rejection.

RESPONSE UNDER 37 CFR 1.116

EXPEDITED PROCEDURE

EXAMINING GROUP 1645

Moreover, definiteness of claim language must be analyzed, not in a vacuum, but in light of the content of the particular application disclosure, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. M.P.E.P. § 2173.02. When the present claims are so examined, it is apparent that the claims circumscribe the claimed subject matter with a reasonable degree of precision and particularity such that one of ordinary skill in the art of organic chemistry could easily determine whether a particular compound is or is not within the scope of the claim. Examination of the instant disclosure reveals that the cited terms *are defined in the specification*. (See, for example, page 10, lines 1 to 13 and page 11, lines 5 to 23 of the specification as filed.) For example, the specification states that “[h]eteroaliphatic groups represented by the group R³ include the aliphatic groups just described but with each group additionally containing one, two, three or four heteroatoms or heteroatom-containing groups.” (Page 10, lines 7 to 13 of the specification as filed). Applicants are therefore at a loss to understand how the Office Action can reasonably suggest that one of ordinary skill in the art would fail to appreciate the intended meaning of the cited terms.

Furthermore, a quick search of the Internet revealed that the terms “cycloaliphatic” and “heteroaliphatic,” for example, are not only familiar to those of ordinary skill in the art, but are used in the art in a manner consistent with their use in the present application. (See attached Appendices B and C). No reason therefore exists to believe that the skilled artisan would have

RESPONSE UNDER 35 U.S.C. § 101
EXPEDITED PRELIMINARY ACTION
EXAMINING GROUP

any difficulty in determining the scope of the claims, and the claims thus meet the requirements of the second paragraph of 35 U.S.C. § 112.

Although the Office Action has alleged that “we do not know what Applicants intend by these unique terms since the prefixes conflict with the stem word aliphatic,” (Office Action dated November 15, 2001, page 5) the Office Action has failed to demonstrate that one of ordinary skill in the art would not understand the meaning of the cited terms and could not determine which groups are encompassed by the cited terms when the claims are read in light of the specification. Accordingly, the rejection for alleged indefiniteness is believed to be improper, and Applicants request withdrawal thereof.

D. Claim 17 has been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for recitation of the phrase “a disease or disorder in a mammal in which the extravasation of leukocytes plays a role.” Applicants respectfully submit that the cited phrase conveys a clear and definite meaning to the skilled artisan. Nevertheless, to advance prosecution and to further clarify the subject matter that Applicants regard as their invention, Claim 17 has been amended to replace “a disease or disorder in which the extravasation of leukocytes plays a role” with a recitation of particular diseases and disorders that can be treated by administration of the claimed compounds. Support for the amendment is found in the specification at, for example, page 22, lines 1 to 11. Applicants submit that the rejection has been obviated, and request withdrawal thereof.

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EXPEDITED PROCEDURE
EXAMINING GROUP 1649

The Office Action asserts that “[c]laimed treatment of multiple sclerosis would raise enablement questions unless Applicants can point to any $\alpha_4\beta_1$ integrin binding inhibitor, which has demonstrated clinical efficacy...” (Office Action dated November 15, 2001, page 8). Applicants direct the Examiner to the attached Drug Report (enclosed herewith as Appendix A) describing a humanized monoclonal antibody specific for the $\alpha_4\beta_1$ integrin, which is currently in Phase III clinical trials for treatment of multiple sclerosis. Applicants therefore submit that treatment of multiple sclerosis with the claimed compounds does not “raise enablement questions.”

Alleged Anticipation

Claims 2 to 10, 12, 13, and 15 to 22 have been rejected under 35 U.S.C. § 102(a) as allegedly anticipated by International Publication No. WO 99/23063 (“the Astles application”). Applicants note, however, that although the Astles application has a purported priority date of October 31, 1997, the application did not publish until May 14, 1999, over 5 months after Applicant's priority date of November 30, 1998. As such, *the Astles application is not available as prior art under § 102(a)*. Applicants accordingly request withdrawal of the rejection.

Furthermore, the statement in the Office Action that “should this reference issue as a US patent, it would be a 102(e) reference against Applicants’ claims” is inappropriate commentary and is not necessarily correct. (Office Action dated November 15, 2001, page 9).

RESPONSE UNDER 37 C.F.R. § 1.102
EXPEDITED PRIORITY REVIEW
EXAMINING PROCEDURE

Miscellaneous

Applicants respectfully request the Examiner to indicate that the documents cited in the Information Disclosure Statement filed January 11, 2000 and the Supplemental Information Disclosure Statement filed May 18, 2001 have been considered by initialing the PTO-1449 forms that were forwarded to the Patent Office when the Information Disclosure Statements were filed, and by forwarding copies of the initialed forms to Applicants for their records. Applicants will forward additional copies of the PTO-1449 forms to the Examiner upon a request to do so.

RESPONSE UNDER 37CFR1.116

EXPEDITED PROCEDURE

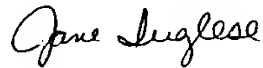
EXAMINING GROUP 1643

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an early and favorable reconsideration of the rejections and an allowance of the pending claims is requested respectfully.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

Respectfully submitted,



Date: **February 15, 2002**

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RESPONSE UNDER 37CFR 1.117

EXPEDITED PROCEDURE

EXAMINING GROUP 1645

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims

Please amend claims 7, 9, 10, 13, 14 and 16 as follows.

7. (Twice amended) A compound according to Claim 16 in which Ar² is [an optionally substituted] a 1,4-phenylene group optionally substituted with one or two atoms or groups -L²(Alk)_iL³(R⁴)_u.

9. (Twice amended) A compound according to Claim 16 in which Ar¹ is [an optionally substituted] a pyrimidinyl, pyridyl or phenyl group optionally substituted with one or more atoms or groups -L²(Alk)_iL³(R⁴)_u.

10. (Amended) A compound according to Claim 9 in which Ar¹ is [an optionally substituted] a pyridyl or phenyl group optionally substituted with one or more atoms or groups -L²(Alk)_iL³(R⁴)_u.

13. (Amended) A compound according to Claim 12 in which R³ is a [an optionally substituted] pyrrolidinyl[,] or thiazolidinyl group optionally substituted with one or more halogen atoms, C₁₋₆alkyl groups, haloC₁₋₆alkyl groups optionally substituted with one or more hydroxyl groups, hydroxyl groups, C₁₋₆alkoxy groups, haloC₁₋₆alkoxy groups, thiol groups, C₁₋

RESPONSE UNDER 37 CFR 1.107

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alkylthio groups, aromatic groups, heteroaromatic groups, or $-(Alk^2)_nR^{10}$ groups, and each nitrogen atom of the pyrrolidinyl or thiazolidinyl group is optionally substituted with a group $-(L^5)_p(Alk^3)_qR^{12}$.

or R^3 is a phenyl, pyrimidinyl or 1,3,5-triazinyl group optionally substituted with one or more atoms or groups $-R^{13a}$ or $-Alk^4(R^{13a})_m$.

14. (Amended) A compound which is:

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-({4-[2-hydroxyethylamino]-6-methoxy-1,3,5-triazin-2-yl}amine)propanoic acid;

3-[(3,5-Dichloroisonicotinoyl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)-amino]phenyl}propanoic acid;

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[(2,6-dimethoxybenzoyl)amino]propanoic acid;

3-({[(4S)-3-Acetyl-1,3-thiazolinan-4-yl]carbonyl}amino-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid;

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-({(2S)-1-[(3,5-dichlorophenyl)sulphonyl]tetrahydro-1-H-pyrrol-2-yl}carbonyl)amino]propanoic acid;

(2RS,3RS)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-({[(2S)-1-[(3,5-dichlorophenyl)sulphonyl]tetrahydro-1-H-pyrrol-2-yl]carbonyl}amino}-2-hydroxypropanoic acid;

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3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[(2-{(2,5-dimethoxyphenyl)thio}-3-pyridinyl)carbonyl)amino]propanoic acid;
and the salts, ~~solvates~~, hydrates and N-oxides thereof.

16. (Amended three times) A compound of formula (1):



wherein

Ar^1 is an [optionally substituted] aromatic or C_{1-9} heteroaromatic group containing one to four heteroatoms selected from oxygen, nitrogen, and sulfur, and is optionally substituted with one or more atoms or groups $-\text{L}^2(\text{Alk})_t\text{L}^3(\text{R}^4)_u$;

L^2 and L^3 , which may be the same or different, is each a covalent bond or a divalent linker atom or group selected from $-\text{O}-$, $-\text{S}-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{O}-$, $-\text{OC}(\text{O})-$, $-\text{C}(\text{S})-$, $-\text{S}(\text{O})-$, $-\text{S}(\text{O})_2-$, $-\text{N}(\text{R}^8)-$, $-\text{CON}(\text{R}^8)-$, $-\text{OC}(\text{O})\text{N}(\text{R}^8)-$, $-\text{CSN}(\text{R}^8)-$, $-\text{N}(\text{R}^8)\text{CO}-$, $-\text{N}(\text{R}^8)\text{C}(\text{O})\text{O}-$, $-\text{N}(\text{R}^8)\text{CS}-$, $-\text{S}(\text{O})_2\text{N}(\text{R}^8)-$, $-\text{N}(\text{R}^8)\text{S}(\text{O})_2-$, $-\text{N}(\text{R}^8)\text{CON}(\text{R}^8)-$, $-\text{N}(\text{R}^8)\text{CSN}(\text{R}^8)-$, and $-\text{N}(\text{R}^8)\text{SO}_2\text{N}(\text{R}^8)-$;

R^8 is a hydrogen atom or a C_{1-6} alkyl group optionally substituted with one or more halogen atoms, hydroxy groups, or C_{1-6} alkoxy groups;

t is zero or the integer 1;

u is an integer 1, 2 or 3;

Alk is an aliphatic or heteroaliphatic chain;

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 EXHIBIT 1
 EXHIBIT 2

R^4 is a hydrogen or halogen atom or a group selected from C_{1-6} alkyl, $-OR^5$, $-SR^5$, $-NR^5R^6$, $-NO_2$, $-CN$, $-CO_2R^5$, $-SO_3H$, $-SO_3R^5$, $-SOR^5$, $-SO_2R^5$, $-OCO_2R^5$, $-CONR^5R^6$, $-OCONR^5R^6$, $-CSNR^5R^6$, $-COR^5$, $-OCOR^5$, $-N(R^5)COR^6$, $-N(R^5)CSR^6$, $-SO_2N(R^5)(R^6)$, $-N(R^5)SO_2R^6$, $-N(R^5)CON(R^6)(R^7)$, $-N(R^5)CSN(R^6)(R^7)$, and $-N(R^5)SO_2N(R^6)(R^7)$; and

R^5 , R^6 , and R^7 , which may be the same or different, is each a hydrogen atom or a straight or branched C_{1-6} alkyl group optionally substituted with one or more halogen atoms, hydroxy groups, or C_{1-6} alkoxy groups;

provided that when t is zero and each of L^2 and L^3 is a covalent bond, then u is the integer 1 and R^4 is other than a hydrogen atom;

L^1 is a covalent bond or a linker atom or group selected from $-CON(R^2)-$, $-S(O)_2N(R^2)-$, $-N(R^2)-$, and $-O-$;

R^2 is a hydrogen atom or a C_{1-3} alkyl group;

Ar^2 is [an optionally substituted] a phenylene group optionally substituted with one or two atoms or groups $-L^2(Alk)_tL^3(R^4)_u$;

R^1 is a group selected from $-NHCOR^3$, $-NHCO_2R^3$, $-NHR^3$, $-NHC(O)OR^3$, $-NHCSR^3$, $-NHCON(R^3)(R^{3a})$, $-NHCO_2N(R^3)(R^{3a})$, and $-NHCSN(R^3)(R^{3a})$;

R^3 is an optionally substituted C_{3-10} cycloaliphatic group, an optionally substituted C_{7-10} polycycloaliphatic group, an optionally substituted C_{3-10} heterocycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from $-O-$, $-S-$, $-C(O)-$, $-C(O)O-$, $OC(O)-$, $-C(S)-$, $-S(O)-$, $-S(O)_2-$, $-N(R^8)-$, $-C(O)NR^8-$,

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EXPIRATION DATE

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-OC(O)N(R⁸)-, -CSN(R⁸)-, -N(R⁸)CO-, -N(R⁸)C(O)O-, -N(R⁸)CS-, -S(O)₂N(R⁸)-, -N(R⁸)S(O)₂-, -N(R⁸)CON(R⁸)-, -N(R⁸)CSN(R⁸)- and -N(R⁸)SO₂N(R⁸)-; an optionally substituted C₇₋₁₀ heteropolycycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, -C(O)NR⁸-, -OC(O)N(R⁸)-, -CSN(R⁸)-, -N(R⁸)CO-, -N(R⁸)C(O)O-, -N(R⁸)CS-, -S(O)₂N(R⁸)-, -N(R⁸)S(O)₂-, -N(R⁸)CON(R⁸)-, -N(R⁸)CSN(R⁸)- and -N(R⁸)SO₂N(R⁸)-; an optionally substituted aromatic group, or an optionally substituted C₁₋₉ heteroaromatic group containing one, two, three or four heteroatoms selected from oxygen, nitrogen, and sulfur;

R^{3a} is a hydrogen atom, an optionally substituted C₁₋₆ aliphatic group, an optionally substituted C₁₋₆ heteroaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, -C(O)NR⁸-, -OC(O)N(R⁸)-, -CSN(R⁸)-, -N(R⁸)CO-, -N(R⁸)C(O)O-, -N(R⁸)CS-, -S(O)₂N(R⁸)-, -N(R⁸)S(O)₂-, -N(R⁸)CON(R⁸)-, -N(R⁸)CSN(R⁸)- and -N(R⁸)SO₂N(R⁸)-, an optionally substituted C₃₋₁₀ cycloaliphatic group, an optionally substituted C₇₋₁₀ polycycloaliphatic group, an optionally substituted C₃₋₁₀ heterocycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, -C(O)NR⁸-, -OC(O)N(R⁸)-, -CSN(R⁸)-, -N(R⁸)CO-, -N(R⁸)C(O)O-, -N(R⁸)CS-, -S(O)₂N(R⁸)-,

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-N(R⁸)S(O)₂-, -N(R⁸)CON(R⁸)-, -N(R⁸)CSN(R⁸)- and -N(R⁸)SO₂N(R⁸)-; an optionally substituted C₇₋₁₀ heteropolycycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, -C(O)NR⁸-, -OC(O)N(R⁸)-, -CSN(R⁸)-, -N(R⁸)CO-, -N(R⁸)C(O)O-, -N(R⁸)CS-, -S(O)₂N(R⁸)-, -N(R⁸)S(O)₂-, -N(R⁸)CON(R⁸)-, -N(R⁸)CSN(R⁸)- and -N(R⁸)SO₂N(R⁸)-; an optionally substituted aromatic group, or an optionally substituted C₁₋₉ heteroaromatic group containing one, two, three or four heteroatoms selected from oxygen, nitrogen, and sulfur;

wherein the optional substituents for the aromatic groups and the heteroaromatic groups of R³ and R^{3a} are selected from one or more atoms or groups R¹³ wherein R¹³ is -R^{13a} or -Alk⁴(R^{13a})_m;

R^{13a} is a halogen atom, or an amino, substituted amino, nitro, cyano, amidino, hydroxyl, substituted hydroxyl, formyl, carboxyl, esterified carboxyl, thiol, substituted thiol, -COR¹⁴-, -CSR¹⁴-, -SO₃H-, -SOR¹⁴-, -SO₂R¹⁴-, -SO₂NH₂-, -SO₂NHR¹⁴-, -SO₂N(R¹⁴)₂-, -CONH₂-, -CSNH₂-, -CONHR¹⁴-, -CSNHR¹⁴-, -CON(R¹⁴)₂-, -CSN(R¹⁴)₂-, -N(R¹¹)SO₂R¹⁴-, -N(SO₂R¹⁴)₂-, -N(R¹¹)SO₂NH₂-, -N(R¹¹)SO₂NHR¹⁴-, -N(R¹¹)SO₂N(R¹⁴)₂-, -N(R¹¹)COR¹⁴-, -N(R¹¹)CONH₂-, -N(R¹¹)CONHR¹⁴-, -N(R¹¹)CON(R¹⁴)₂-, -N(R¹¹)CSNH₂-, -N(R¹¹)CSNHR¹⁴-, -N(R¹¹)CSN(R¹⁴)₂-, -N(R¹¹)CSR¹⁴-, -N(R¹¹)C(O)OR¹⁴-, -SO₂NHet¹-, -CONHet¹-, -CSNHet¹-, -N(R¹¹)SO₂NHet¹-, -N(R¹¹)CONHet¹-, -N(R¹¹)CSNHet¹-, -SO₂N(R¹¹)Het²-, -Het²-, -CON(R¹¹)Het²-, -CSN(R¹¹)Het²-, -N(R¹¹)CON(R¹¹)Het²-, -N(R¹¹)CSN(R¹¹)Het², aryl or heteroaryl group;

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EXPIRATION DATE: 12/1/2018
EXAMINING OFFICE: 10/1/2018

R¹⁴ is an -Alk⁴(R^{13a})_m aryl or heteroaryl group:

NHet¹ is a C₅₋₇cyclicamino group optionally containing one or more -O- or -S- atoms or -N(R¹¹)-, -C(O)- or -C(S)- groups and optionally substituted with one or more substituents as defined for the cycloaliphatic groups of R³ and R^{3a}:

Het² is a monocyclic C₅₋₇carbocyclic group optionally containing one or more -O- or -S- atoms or -N(R¹¹)-, -C(O) or -C(S)- groups and optionally substituted with one or more substituents as defined for the cycloaliphatic groups of R³ and R^{3a}:

Alk⁴ is a straight or branched C₁₋₆alkylene, C₂₋₆alkenylene or C₂₋₆alkynylene chain, optionally interrupted by one, two, or three -O- or -S- atoms or -S(O)_n or -N(R¹⁵)- groups:

R¹⁵ is a hydrogen atom or C₁₋₆alkyl group:

m is zero or an integer 1, 2 or 3;

n is an integer 1 or 2;

wherein the optional substituents for the aliphatic groups and the heteroaliphatic groups of R^{3a} are selected from halogen atoms, hydroxy groups, C₁₋₆alkoxy groups, thiol groups, C₁₋₆alkylthio groups, amino groups, and substituted amino groups;

wherein the optional substituents for the cycloaliphatic, polycycloaliphatic, heterocycloaliphatic and heteropolycycloaliphatic groups of R³ and R^{3a} are selected from halogen atoms, C₁₋₆alkyl groups, haloC₁₋₆alkyl groups optionally substituted with hydroxyl

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groups, hydroxyl groups, C₁₋₆alkoxy groups, haloC₁₋₆alkoxy groups, thiol groups, C₁₋₆alkylthio groups, aromatic groups, heteroaromatic groups, and -(Alk²)_vR¹⁰ groups:

Alk² is a straight or branched C₁₋₃ alkylene chain;

v is zero or an integer 1;

R¹⁰ is a -OH, -SH, -N(R¹¹)₂, -CN, -CO₂R¹¹, -NO₂, -CON(R¹¹)₂, -CSN(R¹¹)₂, -OC(O)N(R¹¹)₂, -C(O)H, -COR¹¹, -OCO₂R¹¹, -OC(O)R¹¹, -C(S)R¹¹, -CSN(R¹¹)₂, -N(R¹¹)COR¹¹, -N(R¹¹)CSR¹¹, -SO₃H, -SOR¹¹, -SO₂R¹¹, -SO₃R¹¹, -SO₂N(R¹¹)₂, -N(R¹¹)SO₂R¹¹, -N(R¹¹)CON(R¹¹)₂, -N(R¹¹)CSN(R¹¹)₂, or -N(R¹¹)SO₂N(R¹¹)₂ group; and

R¹¹ is an atom or group as defined for R⁸ or an optionally substituted cycloaliphatic or heterocycloaliphatic group as defined for R³;

and when R³ is a heterocycloaliphatic group containing one or more nitrogen atoms each nitrogen atom is optionally substituted with a group -(L⁵)_p(Alk³)_qR¹²;

L⁵ is -C(O)-, -C(O)O-, -C(S)-, -S(O)-, -S(O)₂-, -CON(R¹¹)-, -CSN(R¹¹)-, -SON(R¹¹)- or -SO₂N(R¹¹)-;

p is zero or an integer 1;

Alk³ is an optionally substituted aliphatic or heteroaliphatic chain;

q is zero or an integer 1;

R¹² is a hydrogen atom or an optionally substituted cycloaliphatic, heterocycloaliphatic, polycycloaliphatic, polyheterocycloaliphatic, aromatic or heteroaromatic group;

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EXPEDITED PROCEDURE

EXAMINING GROUP 1643

R^a and $R^{a'}$, which may be the same or different, are each independently selected from a hydrogen or halogen atom or an optionally substituted straight or branched alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, haloalkoxy, alkylthio or $-(Alk^b)_mR^b$ group (in which Alk^b is a C_{1-3} alkylene chain, m is zero or the integer 1, and R^b is $-OH$, $-SH$, $-NO_2$, $-CN$, $-CO_2H$, $-CO_2R^c$ (where R^c is an optionally substituted straight or branched C_{1-6} alkyl group), $-SO_3H$, $-SOR^c$, $-SO_2R^c$, $-SO_3R^c$, $-OCO_2R^c$, $-C(O)H$, $-C(O)R^c$, $-OC(O)R^c$, $-C(S)R^c$, $-NR^dR^c$ (where R^d and R^c , which may be the same or different, are each a hydrogen atom or an optionally substituted straight or branched C_{1-6} alkyl group), $-CON(R^d)(R^c)$, $-OC(O)N(R^d)(R^c)$, $-N(R^d)C(O)R^c$, $-CSN(R^d)(R^c)$, $-N(R^d)C(S)R^c$, $-S(O)_2N(R^d)(R^c)$, $-N(R^d)SO_2R^c$, $-N(R^d)CON(R^c)(R^f)$ (where R^f is a hydrogen atom or an optionally substituted straight or branched C_{1-6} alkyl group), $-N(R^d)C(S)N(R^c)(R^f)$ or $-N(R^d)SO_2N(R^c)(R^f)$ group);

Alk^a is an optionally substituted C_{1-6} aliphatic or C_{1-6} heteroaliphatic chain containing one, two, three or four heteroatoms or heteroatom-containing groups selected from $-O-$, $-S-$, $-C(O)-$, $-C(O)O-$, $OC(O)-$, $-C(S)-$, $-S(O)-$, $-S(O)_2-$, $-N(R^8)-$, $-C(O)NR^8-$, $-OC(O)N(R^8)-$, $-CSN(R^8)-$, $-N(R^8)CO-$, $-N(R^8)C(O)O-$, $-N(R^8)CS-$, $-S(O)_2N(R^8)-$, $-N(R^8)S(O)_2-$, $-N(R^8)CON(R^8)-$, $-N(R^8)CSN(R^8)-$, and $-N(R^8)SO_2N(R^8)-$;

wherein the optional substituents for the aliphatic and heteroaliphatic groups of Alk^a are selected from halogen atoms, hydroxy groups, C_{1-6} alkoxy groups, thiol groups, C_{1-6} alkylthio groups, amino groups, and substituted amino groups;

r is zero or the integer 1;

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R is a carboxylic acid (CO₂H), a carboxylic ester group, or carboxylic amide group;
and the salts, [solvates,] hydrates and N-oxides thereof.

17. (Twice amended) A method for the treatment of a mammal suffering from [a disease or disorder in a mammal in which the extravasation of leukocytes plays a role] inflammatory arthritis, multiple sclerosis, allograft rejection, diabetes, inflammatory dermatoses, asthma or inflammatory bowel disease, comprising administering to [a] the mammal [suffering from such a disease or disorder] a therapeutically effective amount of a compound according to Claim 16.

Please cancel claim 18.

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